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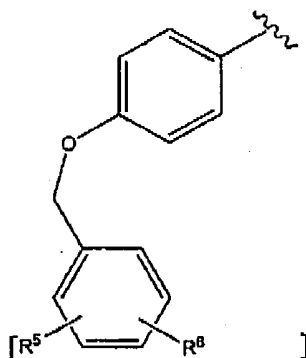
PC10491A

This listing of claims will replace all prior version, and listings, of claims in the application:

Listing of Claims:

Claims 1-15 (canceled).

16. (currently amended) A method for treating a medical condition of the type that is characterized by the destruction of articular cartilage in a human subject; wherein said medical condition comprises joint injury, reactive arthritis, acute pyrophosphate arthritis (pseudogout), psoriatic arthritis, osteoarthritis, or juvenile rheumatoid arthritis; which method comprises administering to the subject having, said condition a therapeutically effective amount of a ~~carboxylic acid hydroxamide derivative having a molecular weight of under 2000 g/mole, wherein said derivative comprises the following substituent:~~

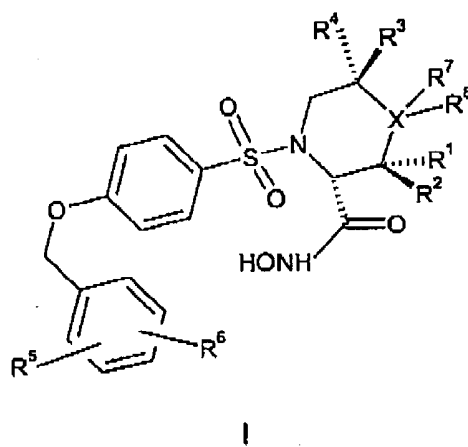


wherein R^5 and R^6 are independent substituents in the ortho, meta, or para positions and are independently selected from the group consisting of hydrogen, halogen, cyano, methyl, and ethyl, and the ~~carboxylic acid hydroxamide derivative exhibits an aggrecanase IC_{50} of less than about 20 nM, said aggrecanase IC_{50} measured by an aggrecanase chondrocyte assay~~ compound represented by formula I:

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or a therapeutically acceptable salt thereof, wherein

X is carbon or nitrogen;

R¹ and R² are independently selected from the group consisting of hydrogen, hydroxy, and methyl, wherein at least one of R¹ and R² is methyl;

R³ and R⁴ are independently selected from the group consisting of hydrogen, hydroxy, and methyl, or R³ and R⁴ may be taken together to form a carbonyl group; and

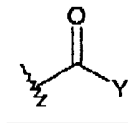
R⁵ and R⁶ are independent substituents in the ortho, meta, or para positions and are independently selected from the group consisting of hydrogen, halogen, cyano, methyl, and ethyl;

with the provisos:

when X is carbon, then R⁷ and R⁸ are both hydrogen and at least one of R¹, R², R³, and R⁴ is hydroxy;

when X is carbon and R⁵ is para-halo, then at least one of R⁶, R³, and R⁴ is not hydrogen;

when X is nitrogen, then R⁸ is not present and R⁷ is hydrogen or a group of the formula:



wherein, Y is -CH₂-NH₂ or -NH-CH₃; and

when X is nitrogen and R⁷ is H, then R³ and R⁴ are taken together to form a carbonyl group.

Claims 17-23 (Canceled).

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24. (New) The method according to claim 16, wherein the medical condition is osteoarthritis.
25. (New) The method of claim 16, wherein X is carbon.
26. (New) The method of claim 25, wherein the medical condition is osteoarthritis.
27. (New) The method of claim 26, wherein the compound is selected from the group consisting of:
- (2*R*,3*R*) 1-[4-(2,4-dichloro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(2,4-dichloro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*R*) 1-[4-(4-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(2-chloro-4-fluoro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*R*) 1-[4-(2-chloro-4-fluoro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*R*) 1-[4-(2-fluoro-4-chloro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*S*) 1-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(4-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(2-methyl-3-fluoro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*R*) 1-[4-(2-fluoro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;

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(2*R*,3*R*) 1-[4-(2-chloro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,3*R*) 1-[4-(2-methyl-3-fluorobenzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,5*R*) 1-[4-(2-methyl-5-chloro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,3*R*) 1-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,3*R*) 1-[4-(2,4-difluoro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,5*R*) 1-[4-(2-fluoro-5-chloro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,3*R*) 1-[4-(2-methyl-5-fluorobenzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide; and
(2*R*,5*R*) 1-[4-(2-bromo-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide.

28. (New) The method of claim 16, wherein X is nitrogen.
29. (New) The method of claim 28, wherein the medical condition is osteoarthritis.
30. (New) The method of claim 29, wherein the compound is selected from the group consisting of:

(2*R*,3*S*) 1-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-4-aminoacetyl-3-methyl-piperazine-2-carboxylic acid hydroxyamide;
(2*R*,3*S*) 1-[4-(4-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-3-methyl-5-oxo-piperazine-2-carboxylic acid hydroxyamide;
(2*R*,3*S*) 4-[4-(2-ethyl-benzyloxy)-benzenesulfonyl]-3-methyl-4-carboxylic acid methylamide-piperazine-2-carboxylic acid hydroxyamide;
(2*R*,3*S*) 4-[4-(5-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-3-methyl-4-carboxylic acid methylamide-piperazine-2-carboxylic acid hydroxyamide;

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(2*R*,3*S*) 1-[4-(2-methyl-5-fluoro-benzyloxy)-benzenesulfonyl]-3-methyl-5-oxo-piperazine-2-carboxylic acid hydroxyamide; and
(2*R*,3*S*) 4-[4-(2,4-difluoro-benzyloxy)-benzenesulfonyl]-3-methyl-4-carboxylic acid methylamide-piperazine-2-carboxylic acid hydroxyamide.